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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/096,589	06/12/1998	ROBERT J. SCHNEIDER	5914-65	1985

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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/22/2002 18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/096,589	Applicant(s) Schneider et al.
	Examiner Rebecca Prouty	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 29, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *47-50* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *47-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *17*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7-29-02 has been entered.

Claims 1-46 have been canceled. Claims 47-50 are at issue and are present for examination.

Applicants' arguments filed on 7-29-02, paper No. 16, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 47-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of inhibiting HBV infection or replication by administering a compound that inhibits enhanced activity of Src kinase which results from the

presence of HBx. The specification fails to describe in any fashion the physical and/or chemical properties or any identifying characteristics or properties other than the functionality of inhibiting enhanced activity of Src kinase resulting from the presence of HBx of the claimed class of substances and fails to identify even a single representative species of such compounds. Moreover, the specification fails to describe how the presence of HBx results in the activation of Src kinase such that the ordinary skilled artisan would have guidance regarding the types of compounds which should be investigated. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants argue that the specification provides a description of the unifying characteristic (i.e., ability to reduce the activation of Src kinase) of the genus of compounds useful in the instant methods and that there is no requirement that they detail each and every compound within the claimed genus. This is not persuasive because the rejection never required the specification to detail each and every compound within the claimed genus but instead to provide a sufficient

description such that members of the genus can be recognized. A sufficient description of a genus requires a precise definition, **such as** by structure, formula, chemical name or physical properties of members of the genus such that one skilled in the art can visualize or recognize the identity of the members of the genus. While these means may as applicants argue constitute a non-exhaustive list of the means by which a sufficient description can be provided, they all provide a mechanism by which one could recognize members of the genus if they had them in hand and applicants specification clearly fails to provide such ability to the skilled artisan whether by these means or by other independent means. Applicants specification fails to provide sufficient information regarding even a single member of the recited genus such that a skilled artisan could not even attempt to practice a **single** embodiment of the claimed invention, yet the claims encompass vastly more than this. As the specification fails to describe **any** representative species it clearly cannot have described the huge genus of methods of the claims.

Applicants further argue that the identification of members of the genus using the assays described in sections 5.5 and 5.5.1 of the specification would not require undue experimentation in

view of the screening assays taught in the specification and the availability of high throughput screening methods in the art. This is not persuasive because the instant rejection is not for lack of enablement but for lack of written description. Description and enablement are separate issues under 35 U.S.C. 112, first paragraph.

Claims 48 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting HBV replication with compounds which reduce Src kinase activation resulting from the presence of HBx, does not reasonably provide enablement for methods of inhibiting HBV replication with any compound which reduces Src kinase activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

Applicants argue that there is no need for the mechanism by which the invention works to be known for the invention to be enabled. While the examiner agrees that the law does not require the mechanism by which the invention works be known, (and the examiner has deemed claims 47 and 49 enabled without any such knowledge), such knowledge is necessary for practice of the

methods of the instant claims without undue experimentation. The only method for screening for compounds within the scope of the instant claims (i.e., that recited in Claim 50) will not specifically identify compounds that inhibit HBV mediated activation of Src kinase. Inhibition of pathways of Src kinase activation distinct from whatever pathway is used by HBV will not inhibit HBV mediated Src kinase activation and thus have no effect on HBV replication. As the specification does not teach the mechanism by which HBV activates Src kinase nor claim use of only specific compounds which are shown to inhibit HBV mediated Src kinase activation and HBV replication (of which no such compounds are in fact disclosed), the only identified method of screening for compounds which would successfully inhibit HBV replication is that recited in Claim 49. Applicants statement that "Necessarily any compound that inhibits Src kinase by any mechanism and at any point in the signaling pathway would work in the claimed methods" is absolutely incorrect. First it should be noted that while any compound that directly inhibits Src kinase activity directly (i.e., kinase enzymatic activity inhibitors) would be expected to be effective at inhibiting HBV, this is not the subject matter of the instant claims. In fact methods of use of such compounds were specifically restricted from the subject matter of the instant claims (and allowed in the parent

application). The instant claims are to use of compounds that inhibit the **activation** of Src kinase, not its activity. As such the means by which it is activated is important as the same enzyme can be activated in multiple different ways by different pathways. Inhibition of one pathway will in no way prevent use of another pathway to achieve Src kinase activation. For example it is well established that the phosphorylation of a variety of different growth factor receptors leads to activation of Src kinase. However, without some showing that HBX (or another HBV protein) activates growth factor receptor phosphorylation *in vivo* one of ordinary skill in the art would have no reasonable expectation that inhibiting phosphorylation of these growth factor receptors (which would inhibit a pathway of Src kinase activation) would have any effect on HBV infection and/or replication. As such merely because a compound is identified by the assay of Claim 50 (as a growth factor receptor phosphorylation inhibitor would be) does **not** mean it would inhibit HBV replication.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more

> than one year prior to the date of application for patent in the United States.

Claims 48-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Moriya et al. The rejection is explained in the previous Office Action.

Applicants argue that Moriya provides no indication that the reduced levels of HBx indeed have a affect on Src kinase activation. This is not persuasive as activation of Src kinase is an inherent effect of the HBx protein and Claim 48 requires only the inhibition of Src kinase enhancement to a level comparable to that which would be present in the absence of HBV. As such the claim does not exclude high levels of Src kinase activation if such levels occur in the absence of HBV. Since HBx gene transcription and translation appears completely inhibited in the transgenic mice (see Figures 1 and 2 of Moriya et al.), Src kinase activation resulting from HBx **must** also be absent and HBV replication dependent thereon inhibited.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 47 and 49-50 (as dependent on Claim 47) are rejected under 35 U.S.C. 103(a) as being unpatentable over Moriya et al.

Moriya et al. teach the inhibition of HBx gene transcription and translation and hepatocellular carcinoma (HCC) by administration of HBx antisense oligonucleotides. While Moriya et al. do not show that these oligonucleotides inhibit activation of Src kinase, this is an inherent effect of the antisense oligonucleotide of Moriya et al. as the oligonucleotide of Moriya inhibited HBx expression such that there is no HBx present to activate Src kinase (see Figures 1 and 2). Moriya et al. do not treat a patient infected with HBV with the antisense oligonucleotides. However, Moriya et al. explicitly suggest that the antisense oligonucleotide would be useful for the inhibition of HBV replication as HBx is considered to be indispensable in establishing infection and regulating viral replication. Therefore, it would have been obvious to one of ordinary skill in the art to treat an HBV infected patient with the antisense

oligonucleotide of Moriya et al. in order to inhibit HBV replication.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652